Severe white matter damage in *SHANK3* deficiency: a human and translational study

Sarah Jesse[1*], Hans-Peter Müller[1], Michael Schoen[2], Harun Asoglu[2], Juergen Bockmann[2], Hans-Juergen Huppertz[3], Volker Rasche[4], Albert C. Ludolph[1,5], Tobias M. Boeckers[2,5], Jan Kassubek[1]

[1]Ulm University, Department of Neurology, Germany
[2]Ulm University, Institute for Anatomy and Cell Biology, Germany
[3]Swiss Epilepsy Clinic, Hospital Lengg, Zurich, Switzerland
[4]Core Facility Small Animal MRI, Ulm University, Ulm, Germany
[5]DZNE site, Ulm, Germany

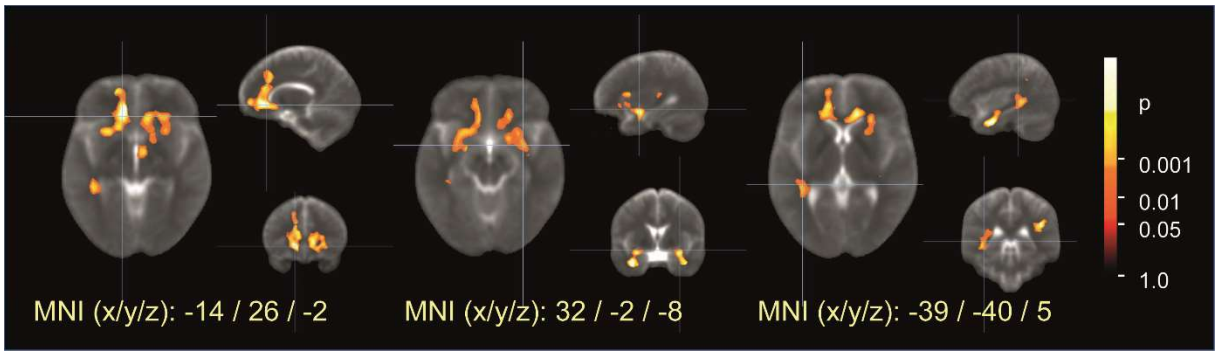
***Corresponding author:**
PD Dr. Sarah Jesse
Department of Neurology, Ulm University
Oberer Eselsberg 45
D-89081 Ulm, Germany
Email: sarah.jesse@uni-ulm.de

Supplementary material

Supplementary Table 1: Upper panel: Cluster coordinates of FA reduction (WBSS) in 9 adolescent and adult PMS patients (14-56 years old) vs. 9 matched controls. **Lower panel:** Results of TFAS of 9 these PMS patients and 9 controls. Significance is marked in yellow with p <0.05

Abbreviations: FA = fractional anisotropy; MNI = Montreal Neurological Institute; PMS = Phelan-McDermid syndrome; TFAS = tractwise fractional anisotropy; WBSS = whole brain-based spatial statistics.

WBSS				
cluster no.	**R/L**	**MNI (x/y/z)**	**Size**	**p values**
1	L	-35 / 2 / -30	15254	< 0.000001
2	R	32 / -3 / 13	11463	< 0.000001
3	L	-41 / -43 / 0	3004	< 0.000001
4	R	42 / -38 / 29	1933	< 0.000001
5	R/L	0 / -27 / -33	1710	< 0.000001
6	L	-47 / -53 / 42	957	< 0.000001
7	R	6 / -8 / -32	661	< 0.000001
8	R	37 / -28 / 7	572	< 0.000001
TFAS				
		PMS	**Controls**	**p values**
uncinate fasciculus		0.283 ± 0.021	0.311 ± 0.021	0.0006
inferior fronto-occipital fasciculus		0.311 ± 0.021	0.351 ± 0.024	0.03
corticostriatal pathway		0.262 ± 0.015	0.279 ± 0.012	0.02



Supplementary Figure 1: Whole brain-based spatial statistics (WBSS) of FA maps at the group level for 9 adolescent and adult PMS patients (14-56 years old) vs 9 matched controls. WBSS of FA maps demonstrated multiple clusters of regional FA reductions at $p<0.05$ (corrected for multiple comparisons, FDR).

Abbreviations: FA = fractional anisotropy; FDR = false-discovery-rate; MNI = Montreal Neurological Institute; PMS = Phelan-McDermid syndrome; WBSS = whole brain-based spatial statistics.